THE USE OF INSTRUMENTAL VARIABLES TO REDUCE CONFOUNDING AND REVERSE-CAUSATION BIAS IN A CROSS-SECTIONAL STUDY FOR PFOA IN RELATION TO CHOLESTEROL

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Background and Aims: Studies of association between an exposure and response in cross-sectional studies may give biased estimates due to unmeasured confounding or reverse causality. However, if we can identify a variable that is (1) associated with the exposure (2) conditionally independent of the response given the exposure; and there is an association between this "instrumental" variable and the response, we may infer a causal relationship between the exposure and the response and derive an unbiased estimate of this relationship. This is illustrated by application to the relationship between serum PFOA and cholesterol.

Methods: The C8 Science Panel Study in the Mid Ohio Valley comprises studies on various outcomes, including cholesterol, in relation to exposure to PFOA in drinking water. Our analyses are based on 56,544 people aged over 18, who had lived in six contaminated water districts, and participated in the survey in 2005-6. Water district was strongly associated with serum PFOA, and thus is a good instrument if populations of each water district have similar distributions of unmeasured risk factors for cholesterol. We assess the use of water district and alternatives as an instrument for measured serum PFOA, to estimate the association between PFOA and cholesterol.

Results: Water district was strongly associated with serum PFOA (Cragg-Donald F statistic = 3699, R^2=0.43). The IV estimated coefficient for association of log serum PFOA with log LDL cholesterol was 0.0072(se= 0.0017). In comparison, a simple linear regression estimate, adjusted as was the IV estimate for age, gender, BMI and medication was 0.015 (se=0.001).

Conclusions: While some types of confounding are avoided by the IV estimate, differences in unmeasured risk factors across water districts may cause bias. In this case both the conventional and IV estimates show an association, which strengthens previous conclusions about the relationship between serum PFOA and cholesterol.